



(19) Europäisches Patentamt  
European Patent Office  
Office européen des brevets



(11) EP 0 558 022 B1

(12)

## EUROPEAN PATENT SPECIFICATION

(45) Date of publication and mention  
of the grant of the patent:  
12.06.1996 Bulletin 1996/24

(51) Int Cl. 6: C12P 17/12  
// (C12P17/12, C12R1:01)

(21) Application number: 93103038.1

(22) Date of filing: 26.02.1993

### (54) Process for preparing 3-cyano-6-hydroxypyridine

Verfahren zur Herstellung von 3-Cyano-6-hydroxypyridin

Procédé de préparation de 3-cyano-6-hydroxypyridine

(84) Designated Contracting States:  
CH DE FR GB IT LI

### (56) References cited:

EP-A- 0 434 035                    EP-A- 0 498 316  
EP-A- 0 519 512                    EP-A- 0 529 653  
EP-A- 0 556 465

(30) Priority: 26.02.1992 JP 39562/92  
31.03.1992 JP 77461/92

- CHEMICAL ABSTRACTS, vol. 107, no. 25, 21 December 1987, Columbus, Ohio, US; abstract no. 228395w, YAMAMOTO, TETSUYA ET AL. 'In vitro conversion of pyrazinamide into 5-hydroxypyrazinamide and that of pyrazinolc acid into 5-hydroxypyrazinolc acid by xanthine oxidase from human liver.' page 15 ;
- CHEMICAL ABSTRACTS, vol. 66, no. 21, 22 May 1967, Columbus, Ohio, US; abstract no. 94996s, HENRYK FOKS ET AL. '2-Pyrazinecarboxylic acid N-oxides. II. Reactions of the derivatives of 2-pyrazinecarboxylic acid N-oxide with acetic anhydride.' page 8898 ;
- DATABASE WPI Section Ch, Week 9250, Derwent Publications Ltd., London, GB; Class B02, AN 92-409786 & JP-A-4 304 893 (IKEDA SHOKUKEN) 28 October 1992
- CHEMICAL ABSTRACTS, vol. 120, no. 13, 28 March 1994, Columbus, Ohio, US; abstract no. 161783u, page 960 ;

(43) Date of publication of application:  
01.09.1993 Bulletin 1993/35

(73) Proprietor: Mitsubishi Chemical Corporation  
Chiyoda-ku Tokyo (JP)

### (72) Inventors:

- Yasuda, Mari  
Yokohama-shi, Kanagawa-ken (JP)
- Ohkishi, Haruyuki  
Machida-shi, Tokyo-to (JP)
- Sato, Katsutoshi  
Machida-shi, Tokyo-to (JP)
- Morimoto, Yuuki  
Machida-shi, Tokyo-to (JP)
- Nagasawa, Toru  
Nagoya-shi, Aichi-ken (JP)

### (74) Representative:

Hansen, Bernd, Dr. Dipl.-Chem. et al  
Hoffmann, Ettie & Partner  
Patent- und Rechtsanwälte,  
Postfach 81 04 20  
81904 München (DE)

EP 0 558 022 B1

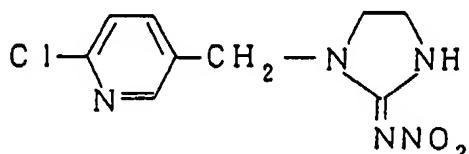
Note: Within nine months from the publication of the mention of the grant of the European patent, any person may give notice to the European Patent Office of opposition to the European patent granted. Notice of opposition shall be filed in a written reasoned statement. It shall not be deemed to have been filed until the opposition fee has been paid. (Art. 99(1) European Patent Convention).

**Description**

The present invention relates to a process for preparing 6-hydroxy nitrogen-containing 6-membered ring compounds. More particularly, this invention relates to a process for preparing 3-cyano-6-hydroxypyridine.

Various nitrogen-containing 6-membered ring compounds such as dihydropyridines, nicotinic acids and the like, can be important synthetic intermediates for preparing medicines, agricultural chemicals, dyestuffs or the like. For example, a new type of insecticides which act on nicotinic acid receptors have recently been studied, and Imidacloprid (Nippon Tokushu Noyaku Co.) represented by the following formula is one of the new insecticides.

10



15

As the intermediates for the preparation of Imidacloprid, 3-chloromethyl-6-chloropyridine is very important.

Various synthetic routes for preparing the pyridines having substituents at 3- and 6-positions have been intensively studied thus far. However, there is no method for selectively introducing a substituent at 6-position of 3-substituted pyridine by the method of organic chemistry. On the other hand, a process for introducing a hydroxy group at 6-position of nicotinic acid using a microorganism belonging to genus Pseudomonas, genus Bacillus or genus Achromobacter, which is capable of decomposing nicotinic acid, has been described in Japanese Patent Publication (KOKAI) Nos. 60-196193 and 60-196194. However, it is necessary to express the activity more effectively for putting the above process into practical use.

25 EP-A-0 434 035 discloses a microbiological method for preparing 6-hydroxynicotinic acid wherein nicotinic acid is enzymatically hydroxylised in the presence of a microorganism selected from Pseudomonas, Bacillus or Achromobacter.

Microorganisms used in the present invention illustratively include a microorganism selected from the microorganisms belonging to Genus Agrobacterium, Genus Arthrobacter, Genus Bordetella, Genus Brevibacterium, Genus Pseudomonas, Genus Achromobacter, Genus Comamonas, Genus Erwinia, Genus Bacterium, Genus Corynebacterium, Genus Serratia, Genus Sarcina, Genus Xanthobacter, Genus Alcaligenes, Genus Flavobacterium Genus and Genus Micrococcus. These microorganisms which have been physico-chemically treated can also be employed. Microorganisms usable in the process of the present invention should not be restricted to the above-listed organisms as far as they have an ability to selectively introduce a hydroxyl group at the 6-position of 3-cyanopyridine.

35 The microorganisms belonging to Genus Agrobacterium illustratively include Agrobacterium radiobacter, Agrobacterium tumefaciens, Agrobacterium viscosum and the like. More specifically, there are exemplified Agrobacterium radiobacter NRRL B-11291 (Agricultural Research Service Culture Collection), Agrobacterium tumefaciens IAM 13129 (Research Institute of Applied Microbiology, Tokyo University), Agrobacterium viscosum IFO 13652 (Institute for Fermentation, Osaka), etc.

40 The microorganisms belonging to Genus Arthrobacter illustratively include Arthrobacter globiformis, Arthrobacter fragilis and the like. More specifically, there are exemplified Arthrobacter globiformis IFO 12137 (Institute for Fermentation, Osaka), Arthrobacter fragilis FERM P-4350 (Fermentation Research Institute, Agency of Industrial Science and Technology), etc.

45 The microorganisms belonging to Genus Bordetella illustratively include Bordetella bronchiseptica and the like. More specifically, there are exemplified Bordetella bronchiseptica ATCC 4617 (American Type Culture Collection) etc.

The microorganisms belonging to Genus Brevibacterium illustratively include Brevibacterium butanicum, Brevibacterium ketoglutamicum and the like. More specifically, there are exemplified Brevibacterium butanicum ATCC 21196 (American Type Culture Collection), Brevibacterium ketoglutamicum ATCC 15587 (American Type Culture Collection), etc.

50 The microorganisms belonging to Genus Pseudomonas illustratively include Pseudomonas dacunhae, Pseudomonas maltophilia, Pseudomonas chlororaphis, Pseudomonas hydantoinophilum, Pseudomonas putida, Pseudomonas fluorescens and the like. More specifically, there are exemplified Pseudomonas dacunhae ATCC 13261 (American Type Culture Collection), Pseudomonas maltophilia ATCC 13637 (American Type Culture Collection), Pseudomonas chlororaphis IFO 3904 (Institute for Fermentation, Osaka), Pseudomonas hydantoinophilum FERM P-4347 (Fermentation Research Institute, Agency of Industrial Science and Technology), Pseudomonas putida ATCC 21244 (American Type Culture Collection), Pseudomonas fluorescens IFO 3903 (Institute for Fermentation, Osaka), etc.

55 The microorganisms belonging to Genus Achromobacter illustratively include Achromobacter xerosis and the like. More specifically, there are exemplified Achromobacter xerosis IFO 12668 (Institute for Fermentation, Osaka), etc.

The microorganisms belonging to Genus Comamonas illustratively include Comamonas acidovorans, Comamonas testosteronei and the like. More specifically, there are exemplified Comamonas acidovorans NCIMB 9289 (National Collection of Industrial And Marine Bacteria Ltd.), Comamonas testosteronei ATCC 11996 (American Type Culture Collection), etc.

- 5 The microorganisms belonging to Genus Erwinia illustratively include Erwinia herbicola and the like. More specifically, there are exemplified Erwinia herbicola ATCC 21434 (American Type Culture Collection), etc.

The microorganisms belonging to Genus Bacterium illustratively include Bacterium cyclo-oxydans and the like. More specifically, there are exemplified Bacterium cyclo-oxydans ATCC 12673 (American Type Culture Collection), etc.

- 10 The microorganisms belonging to Genus Corynebacterium illustratively include Corynebacterium xerosis and the like. More specifically, there are exemplified Corynebacterium xerosis NCTC 9755 (National Collection of Type Cultures), etc.

The microorganisms belonging to Genus Serratia illustratively include Serratia liquefaciens, Serratia marcescens and the like. More specifically, there are exemplified Serratia liquefaciens IFO 12979 (Institute for Fermentation, Osaka), Serratia marcescens IFO 3054 (Institute for Fermentation, Osaka), Serratia marcescens IFO 12648 (Institute for Fermentation, Osaka), etc.

- 15 The microorganisms belonging to Genus Sarcina illustratively include Sarcina lutea and the like. More specifically, there are exemplified Sarcina lutea ATCC 9341 (American Type Culture Collection), etc.

The microorganisms belonging to Genus Xanthobacter illustratively include Xanthobacter flavus and the like. More specifically, there are exemplified Xanthobacter flavus NCIMB 10071 (National Collections of Industrial And Marine Bacteria Ltd.), etc.

- 20 The microorganisms belonging to Genus Alcaligenes illustratively include Alcaligenes eutrophus, Alcaligenes aquamarinus, Alcaligenes faecalis and the like. More specifically, there are exemplified Alcaligenes eutrophus ATCC 17699 (American Type Culture Collection), Alcaligenes aquamarinus FERM P-4229 (Fermentation Research Institute, Agency of Industrial Science and Technology), Alcaligenes faecalis IFO 13111 (Institute for Fermentation, Osaka), etc.

25 The microorganisms belonging to Genus Flavobacterium illustratively include Flavobacterium suaveolens, Flavobacterium aminogenes, Flavobacterium arborescens, Flavobacterium dehydrogenans, Flavobacterium heparinum and the like. More specifically, there are exemplified Flavobacterium suaveolens IFO 3752 (Institute for Fermentation, Osaka), Flavobacterium aminogenes FERM P-3134 (Fermentation Research Institute, Agency of Industrial Science and Technology), Flavobacterium arborescens IFO 3750 (Institute for Fermentation, Osaka), Flavobacterium dehydrogenans ATCC 13930 (American Type Culture Collection), Flavobacterium heparinum IFO 12017 (Institute for Fermentation, Osaka), etc.

- 30 The microorganisms belonging to Genus Micrococcus illustratively include Micrococcus varians, Micrococcus morrhuae and the like. More specifically, there are exemplified Micrococcus varians IAM 1314 (Institute of Applied Microbiology, The University of Tokyo), Micrococcus morrhuae IAM 1711 (Institute of Applied Microbiology, The University of Tokyo), etc.

35 Nutrients necessary for cultivation of these microorganisms have no limitation, and conventional nutrients used for microorganisms can be used. For example, carbon sources include sugars such as glucose, sucrose, fructose, glycerol, sorbitol, molasses, starch hydrolysate or the like, and organic acids such as acetic acid, fumaric acid or the like. Nitrogen sources include nitrates, ammonium salts, corn steep liquor, yeast extract, meat extract, yeast powder, 40 soy bean hydrolysate, cotton seed dust, polypeptone, Benton and the like. Minerals include potassium phosphate, calcium phosphate, sodium phosphate, magnesium sulfate, manganese sulfate, sodium chloride and the like. Minerals such as sources of iron ion, cobalt ion, copper ion or the like may be favorably added to the culture for inducing the production of enzymes.

- 45 Cultivation may be favorably effected under aerobic conditions at temperature from 20 to 40°C, preferably 30 to 35°C, at pH 4.0 to 9.0, preferably pH 5.0 to 7.0 over a period of 20 to 24 hours, until population of microorganisms increases up to about OD<sub>660</sub> 5 to OD<sub>660</sub> 40.

The "physico-chemically treated microorganism" in the present invention means the microorganism extracts, pulverized microorganism, and their purified product obtained by known methods such as separation by ammonium sulfate, ion exchange chromatography, gel filtration or the like. In the process of the present invention, the 3-cyanopyridine 50 may be reacted with a microorganism itself (living cell or dried cell) or physico-chemically treated microorganism.

- The microorganism obtained by the cultivation or physico-chemically treated microorganism can be fixed on a gel, such as polyacrylamide gel, photo-crosslinking resin, carrageenan or the like, and then allowed to react with the 3-cyanopyridine.

When 3-cyanopyridine is allowed to react with a microorganism per se, it may be added to the microorganism 55 which has been sufficiently grown. Appropriate concentration of 3-cyanopyridine is between 0.1% by weight and the saturated concentration, preferably 1.0 to 5.0% by weight. The reaction is carried out at temperature from 20 to 50°C, preferably 30 to 40°C, at pH 4.0 to 9.0, preferably 5.0 to 7.0, over a period of 2 to 24 hours, ordinarily 20 to 24 hours, under aerobic conditions and with stirring.

When 3-cyanopyridine is allowed to react with physico-chemically treated microorganism, the compound is added to an aqueous solution, such as 0.01 to 1M phosphate buffer (pH 6 - 9) containing about 2 to 15 mg (protein weight) of microorganism extract or pulverized microorganism.

When the microorganism per se or treated microorganism is fixed, the 3-cyanopyridine is reacted with the fixed microorganism under the above-mentioned conditions in a reactor equipped with a stirrer. Alternatively, a liquid containing the nitrogen-containing 6-membered ring compound is passed through a column filled with the fixed microorganism.

Efficiency of the hydroxylation can be raised in the process of the present invention by effecting the reaction in the presence of phenazine methosulfate. In this case, phenazine methosulfate (N-methylphenazonium methosulfate or 5-methylphenazinium methyl sulfate) is needed to exist in the reaction mixture. More specifically, phenazine methosulfate may be added together with 3-cyanopyridine at a time for the reaction with the microorganism per se or treated microorganism. Appropriate concentration of phenazine methosulfate in the reaction mixture is 1 to 100 mM, preferably 5 to 100 mM.

The aqueous medium used in the present invention may be water or a buffer such as acetate buffer, phosphate buffer or the like. An excessive amount of said aqueous medium for 3-cyanopyridine as a substrate is preferred.

The 3-cyano-6-hydroxypyridine thus obtained can be extracted in a conventional manner from the reaction mixture with a solvent such as methanol, water or the like, and purified by column chromatography filled with ODS resin or the like.

The 3-cyano-6-hydroxypyridine, obtained in the present invention are useful as intermediates for the preparation of medicines, agricultural chemicals, dyestuffs or the like. For example, 3-cyano-6-hydroxypyridine can be easily converted by a conventional method into 3-chloromethyl-6-hydroxypyridine, an intermediate for agricultural chemicals.

The following detailed Examples are presented by way of illustration of certain specific embodiments of the invention. The Examples are representative only and should not be construed as limiting in any respect.

25 Example 1

To an Erlenmeyer flask equipped with navel was filled a nutrient solution containing 1 g of yeast extract, 1 g of glucose, 0.3 g of  $K_2 HPO_4$ , 0.1 g of  $KH_2 PO_4$ , 1 mg of  $FeSO_4$ , 50 mg of  $MgSO_4$ , 1 mg of  $MnSO_4$  and 100 ml of water, and the resultant mixture was sterilized at 120°C for 20 minutes. After cooling to 30°C, the mixture was added with separately sterilized 1 mg of  $CuSO_4$  and 0.2 g of 3-cyanopyridine as an inducer. One of the microorganisms listed in Table 1 which was incubated on nutrient agar medium for 24 hours was inoculated into the above mixture with a platinum loop, and the mixture was incubated at 30°C for 24 hours using a rotary shaker of 160 rpm. After 24 hours, the broth was recovered and centrifuged. The cell separated were suspended in and washed with 0.02 mol of an acetate buffer (pH 5.5) and centrifuged to give a resting cell. To a 100 ml reactor was added 20 ml of 1.0% 3-cyanopyridine (pH 5.5), and the mixture was heated at 30°C, and mixed with the resting cell obtained above. The resultant mixture was stirred sufficiently for 24 hours to give 3-cyano-6-hydroxypyridine. The product was identified by means of HPLC, IR and  $^1H$ -NMR. Table 1 shows the results.

Table 1.

40	Microorganisms used	Yield (mg)
	<u>Achromobacter xerosis</u> (IFO 12668)	2.0
	<u>Agrobacterium radiobacter</u> (NRRL B-11291)	1.0
	<u>Alcaligenes eutrophus</u> (ATCC 17699)	3.0
45	<u>Alcaligenes aquamarinus</u> (FERM P-4229)	2.0
	<u>Alcaligenes faecalis</u> (IFO 13111)	2.0
	<u>Arthrobacter globiformis</u> (IFO 12137)	3.0
	<u>Arthrobacter fragilis</u> (FERM P-4350)	2.0
50	<u>Bacterium cyclo-oxydans</u> (ATCC 12673)	13.0
	<u>Bordetella bronchiseptica</u> (ATCC 4617)	10.0
	<u>Brevibacterium butanicum</u> (ATCC 21196)	12.0
	<u>Brevibacterium ketoglutaricum</u> (ATCC 15587)	2.0
	<u>Corynebacterium xerosis</u> (NCTC 9755)	19.0
55	<u>Erwinia herbicola</u> (ATCC 21434)	2.0
	<u>Flavobacterium suaveolens</u> (IFO 3752)	1.0
	<u>Micrococcus varians</u> (IAM 1314)	1.0

Table 1. (continued)

Microorganisms used	Yield (mg)
<u>Micrococcus morrhuae</u> (IAM 1711)	1.0
<u>Comamonas acidovorans</u> (NCIMB 9289)	72.0
<u>Comamonas testosteroni</u> (ATCC 11996)	24.0
<u>Pseudomonas dacunhae</u> (ATCC 13261)	12.0
<u>Pseudomonas maltophilia</u> (ATCC 13637)	19.0
<u>Pseudomonas chlororaphis</u> (IFO 3904)	1.0
<u>Pseudomonas hydantoinophilum</u> (FERMP-4347)	5.0
<u>Pseudomonas putida</u> (ATCC 21244)	1.0
<u>Sarcina lutea</u> (ATCC 9341)	3.0
<u>Serratia liquefaciens</u> (IFO 12979)	1.0
<u>Serratia marcescens</u> (IFO 3054)	1.0
<u>Serratia marcescens</u> (IFO 12648)	2.0
<u>Xanthobacter flavus</u> (NCIMB 10071)	1.0

<sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) δ: 6.42 (1H, d, J<sub>4,5</sub> = 9.9 Hz, H-5), 7.67 (1H, dd, J<sub>4,5</sub> = 9.9 Hz, J<sub>2,4</sub> = 2.4 Hz, H-4), 8.26 (1H, d, J<sub>2,4</sub> = 2.4 Hz, H-2), 12.40 (1H, bs, OH)

#### Example 2

<sup>25</sup> Sakaguchi flask was filled with a nutrient solution (pH 7.0) containing 1 g of meat extract, 1 g of malic acid, 0.1 g of K<sub>2</sub>HPO<sub>4</sub>, 1 g of nicotinic acid, 500 mg of MgSO<sub>4</sub>·7H<sub>2</sub>O and 100 ml of water, and the content was sterilized at 120°C for 20 minutes. After cooling to 30°C, 2 ml of a sterilized metallic solution (shown in Table 2) was added. After incubation for 24 hours on nutrient agar medium, one platinum loop of each Serratia marcescens (IFO 12648) and Pseudomonas fluorescens (IFO 3903) was inoculated and incubated at 30°C for 36 hours in a reciprocal shaker. After recovering the cultivated product, the cells were centrifuged. The separated cells were suspended in and washed with 0.1 mol of a phosphate buffer (pH 7.0) and centrifuged to give the cells. The resultant cells were pulverized by supersonic wave and subjected to ultracentrifugation. The resultant precipitate was mixed with and suspended in 0.3% Triton X and 0.1% cetylpyridinium chloride on ice for 1 hour and again subjected to ultracentrifugation. The supernatant was used as a crude enzyme solution. The precipitate was again subjected to the same procedure, and the supernatant was added to the crude enzyme solution. The crude enzyme solution was purified by column chromatography on DEAE Sephadex, Phenyl Sepharose, Butyl Toyopearl or the like.

<sup>30</sup> The reaction was initiated by mixing 100 μl of the enzyme solution with 1.5 mM DCIP (2,6-Dichloroindophenol), 2.0 ml of 0.1 M phosphate buffer (pH 7.0), 100 μl of 3.0 mM PMS (phenazine methosulfate), and 500 μl of 2 mM - 5 mM substrate solution as shown in Table 2. After finishing the reaction at 30°C for 1 minute, an activity was assayed by measuring the change of absorbance at 600 nm. Table 3 shows the test results.

Table 2.

Composition of the Metallic Solution	
Metal	/L of DW
CaCl <sub>2</sub> ·2H <sub>2</sub> O	400 mg
H <sub>3</sub> BO <sub>3</sub>	500 mg
CuSO <sub>4</sub> ·5H <sub>2</sub> O	40 mg
KI	100 mg
FeSO <sub>4</sub> ·7H <sub>2</sub> O	200 mg
MnSO <sub>4</sub> ·7H <sub>2</sub> O	400 mg
ZnSO <sub>4</sub> ·7H <sub>2</sub> O	400 mg
H <sub>2</sub> MoO <sub>4</sub> ·2H <sub>2</sub> O	200 mg
HCl	20 ml

Table 3.

Substrate	S. marcescens	P. fluorescens
	IFO 12648	IFO 3903
3-Cyanopyridine	μM 33	μM 11

5

N.D.: not determined

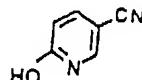
10 It was found from the results of Examples 1 and 2 that the hydroxy group can be selectively introduced at the 6-position of 3-cyanopyridine by the action of the microorganisms used.

15

**Claims**

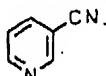
20

1. A process for preparing 3-cyano-6-hydroxypyridine of the formula:



25

which process comprises reacting 3-cyanopyridine of the formula:



30

with a microorganism selected from the group consisting of Genus Agrobacterium, Genus Arthrobacter, Genus *Bordetella*, Genus *Brevibacterium*, Genus *Pseudomonas*, Genus *Achromobacter*, Genus *Comamonas*, Genus *Erwinia*, Genus *Bacterium*, Genus *Corynebacterium*, Genus *Serratia*, Genus *Sarcina*, Genus *Xanthobacter*, Genus *Alcaligenes*, Genus *Flavobacterium*, and Genus *Micrococcus*, or with an enzyme derived from any of the said microorganisms in an aqueous medium, and recovering 3-cyano-6-hydroxypyridine from the medium.

35

2. Process according to claim 1, in which the reaction is effected in the presence of phenazine methosulfate.

40

**Patentansprüche**

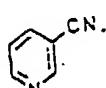
45

1. Verfahren zur Herstellung von 3-Cyano-6-hydroxypyridin der Formel:



50

wobei man 3-Cyanopyridin der Formel:



55

mit einem Mikroorganismus aus der Gruppe aus Genus *Agrobacterium*, Genus *Arthrobacter*, Genus *Bordetella*, Genus *Brevibacterium*, Genus *Pseudomonas*, Genus *Achromobacter*, Genus *Comamonas*, Genus *Erwinia*, Genus *Bacterium*, Genus *Corynebacterium*, Genus *Serratia*, Genus *Sarcina*, Genus *Xanthobacter*, Genus *Alcaligenes*, Genus *Flavobacterium* und Genus *Micrococcus* oder mit einem aus jedem der genannten Mikroorganismen abgeleiteten Enzym in einem wässrigen Medium zur Reaktion bringt und 3-Cyano-6-hydroxypyridin aus dem Medium gewinnt.

2. Verfahren gemäß Anspruch 1.

wobei die Reaktion in der Gegenwart von Phenazinmethosulfat durchgeführt wird.

**Revendications**

5

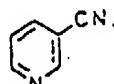
1. Procédé pour la préparation de la 3-cyano-6-hydroxypyridine de formule :

10



lequel procédé comprend la réaction de la 3-cyanopyridine de formule :

15



20

avec un micro-organisme choisi parmi le genre Agrobacterium, le genre Arthrobacter, le genre Bordetella, le genre Brevibacterium, le genre Pseudomonas, le genre Achromobacter, le genre Comamonas, le genre Erwinia, le genre Bacterium, le genre Corynebacterium, le genre Serratia, le genre Sarcina, le genre Xanthobacter, le genre Alcaligenes, le genre Flavobacterium et le genre Micrococcus, ou avec une enzyme dérivée de l'un quelconque desdits micro-organismes, dans un milieu aqueux, et la récupération à partir du milieu de la 3-cyano-6-hydroxypyridine.

25

2. Procédé selon la revendication 1, dans laquelle la réaction est effectuée en présence de méthosulfate de phéna-

zine.

30

35

40

45

50

55